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# facsimile transmittal

To: Dockets Management Branch Fax: (301) 827-6870  
From: Wyeth-Ayerst Laboratories Fax: (610) 964-3832  
Date: September 10, 1999 Pages: 4  
Re: Docket No. 99N-0193

☐ Urgent ☒ For Review ☐ Please Comment ☐ Please Reply ☐ Please Recycle

Notes: Reference is made to Wyeth-Ayerst Laboratories' letter, dated September 9, 1999,  
providing comments on the Proposed Rule: Supplements and Other Changes to an Approved  
Application, wherein we reference the letter dated April 11, 1996 from Roger Williams, M.D.  
We, hereby, are amending our submission package to include a copy of this letter. We  
respectfully request that the Roger Williams letter included in this facsimile be attached to the  
end of our letter. We also have attached a copy of the first page of our six page letter for  
identification purposes.

*Karel F. Bernady*

Karel F. Bernady, Ph.D.

CONFIDENTIAL

99N-0193

ANDI

WYETH-AYERST  RESEARCH

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Division of American Home Products Corporation

VERN G. DEVRIES, Ph.D.  
ASSISTANT VICE PRESIDENT  
U.S. REGULATORY AFFAIRS

September 9, 1999

Dockets Management Branch  
Food and Drug Administration  
HFA-305, Room 1061  
5630 Fishers Lane  
Rockville, MD 20852

Re: {Docket No. 99N-0193}

Proposed Rule: Supplements and Other Changes to an Approved Application

Dear Sir or Madam:

On behalf of American Home Products, a diversified manufacturer of pharmaceutical, over-the-counter and biological drug products, we welcome the opportunity to comment on the Proposed Rule: Supplements and Other Changes to an Approved Application. This letter represents the combined comments of Wyeth-Ayerst Laboratories, Wyeth-Ayerst Research, Whitehall-Robins Health Care, ESI-Lederle, Wyeth-Lederle Vaccines and Pediatrics, and Genetics Institute.

The Food and Drug Administration's (FDA) proposed language from the Federal Register notice is italicized in this letter and identified by section. Our suggestions for revised language appear in standard type.

**General Comments:**

The Agency's proposed rule imposes additional regulatory burdens on applicants in reporting changes to an approved application. Examples of these increased reporting requirements are given herein. It is our opinion that these new regulatory requirements are beyond the intent of Congress, when it drafted and approved the "Food and Drug Administration Modernization Act of 1997" (FDAMA). We ask the Agency to revise the proposed rule to remove the additional regulatory burdens and issue a rule in keeping with Congress' intent.

**§314.3(b)**

\* \* \* \* \*

*Validate the effects of the change means to assess the effect of a manufacturing change on the identity, strength, quality, purity, or potency of a drug as these factors relate to the safety or effectiveness of the drug.*

We recommend that the word "assess" replace the word "validate" and "determine" replace "assess" in this section to read: Assess the effects of the change means to determine the effect of a manufacturing change on the identity, strength, quality, purity, or potency of a drug as these factors relate to the safety or effectiveness of the drug.



## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

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Dear Sir or Madam:

A notice of the availability of a guidance entitled *Immediate Release Solid Oral Dosage Forms; Scale-up and Postapproval Changes (SUPAC-IR)* was issued by the Center for Drug Evaluation and Research on November 30, 1995 (FR Vol. 60, No. 230, pp. 61638 - 61643). A copy of the Guidance may be obtained from the Consumer Affairs Branch, HFD 8, Center for Drug Evaluation and Research (CDER), 5600 Fishers Lane, Rockville, MD 20857 (Phone: 301-594-1012). An electronic version is available via Internet by connecting to the CDER file transfer Protocol (FTP) server (DCVS2.CDER.FDA.GOV).

This guidance provides filing requirements that are in some cases different than previously described under 21 CFR 314.70(b) and 314.70(c). Implementation and correct interpretation by the Agency and industry will depend greatly on a clear description of both the purpose of and basis for the submissions made using the guidance. This description is necessary in order to aid in determining whether the correct type of submission has been made and to allow for ready monitoring of the impact and utilization of the guidance. For this reason we are requesting that all SUPAC-IR submissions contain the following information:

1. A brief, explicit description of the change addressed by the submission. For supplements, including Changes Being Effected (CBE), this should be included in the cover letter. For annual reports, it should be in the summary description of the changes described in the report.
2. A reference identifying the specific section of the SUPAC-IR guidance used as the basis for the submission.
3. A designation on the exterior envelope and above the body of the cover letter (for supplements) and on the Form 2252 (for annual reports) to indicate that the submission is based on the SUPAC-IR guidance.

The attached sample cover letter is intended as an example of the submission summary information requested for pre-approval and CBE supplements and also of the format for the additional information specific to SUPAC-IR.

We request that your submissions use a format similar to this example so that information necessary to allow proper administrative and technical evaluation is clearly presented.

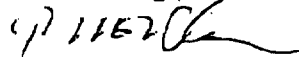
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APR 17 1996

Karel F. Bernady, Ph.D.  
U.S. Regulatory Affairs

In addition, in order to eliminate the uncertainty that may exist regarding the role of Field inspections in SUPAC CBE site changes, the following comments are provided. The SUPAC guidance does not eliminate inspection requirements for site changes, nor requirements that firms have adequate process validation to support all changes. On page 13 of the guidance is the statement "New manufacturing locations should have a satisfactory current Good Manufacturing Practice (CGMP) inspection." This statement also applies to moves between existing facilities. Firms should file these CBE supplements for the proposed site only when they have a satisfactory GMP status. If it is determined that this is not the case, the applicant will be notified that the submission is no longer considered a Changes Being Effected supplement and has been reclassified to require prior approval. In this circumstance, the submitted change may not be made until the submission is approved. Products manufactured and distributed under a denied CBE supplement may be at risk. If a firm is uncertain about its status, the District and/or Review Division should be contacted for clarification before the CBE submission is made.

Sincerely,



Roger L. Williams, M.D.  
Deputy Center Director for  
Pharmaceutical Science  
Center for Drug Evaluation and Research